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1 RECORD OF ORAL HEARING  
2  
3 UNITED STATES PATENT AND TRADEMARK OFFICE  
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5  
6 BEFORE THE BOARD OF PATENT APPEALS  
7 AND INTERFERENCES  
8

9  
10 *Ex parte* STUART L. SCHREIBER and GERALD R. CRABTREE  
11

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13 Appeal 2007-3483  
14 Application 09/834,424  
15 Technology Center 1600  
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18 Oral Hearing Held: September 9, 2008  
19

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22 Before TONI R. SCHEINER, DEMETRA J. MILLS,  
23 and ERIC B. GRIMES, *Administrative Patent Judges*.  
24

25 ON BEHALF OF THE APPELLANT:

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31  
32 PROCEEDINGS

33 MS. BOBO-ALLEN: Good morning.

34 JUDGE SCHEINER: Good morning.

1 MS. BOBO-ALLEN: Calendar Number 1, Appeal Number 2007-  
2 3483. Mr. Berstein.

3 JUDGE SCHEINER: Thank you.

4 MS. BOBO-ALLEN: Um-hum.

5 JUDGE SCHEINER: Good morning.

6 MR. BERSTEIN: Good morning.

7 JUDGE SCHEINER: Would you like to introduce your colleague for  
8 the record?

9 UNIDENTIFIED: Your Honor, I'm not actually moving in.

10 JUDGE SCHEINER: That's okay.

11 MR. BERSTEIN: So I'm David Berstein and I'm Chief Patent  
12 Counsel at Ariad Pharmaceuticals. We're the exclusive licensee of this  
13 Patent Application. With me is Brenda Jarrell who worked closely with me  
14 on the prosecution. And I've never done this before, so I'm a little  
15 nervous --

16 JUDGE SCHEINER: Don't be.

17 MR. BERSTEIN: -- and I'm not sure what the formalities are. If I  
18 have any gaffs, it's unintentional. What I want to -- so there are two  
19 outstanding rejections. There's an art rejection and a written description of  
20 the invention rejection.

21 The art rejection is, to us -- we feel that we've traversed it pretty  
22 clearly in our papers, and my suggestion is that I would spend most of my  
23 time on the written description part of it, which I think raises much more  
24 interesting questions.

25 JUDGE SCHEINER: That's fine.

1           MR. BERSTEIN: Okay. So, the Examiner -- this is one of those  
2 cases where the Examiner felt that the invention wasn't disclosed in a way  
3 that conveyed possession of the invention by our inventors to the reader, the  
4 skilled artisan reading this document. And so we know from the case law,  
5 the evolution of the case law, the written description generally requires some  
6 level of detail in the description to convey that possession to the reader, and  
7 it's been explored in lots of different contexts. You know, the DNA famous  
8 cases and those different cases, those different inventions and circumstances  
9 have lead to a number of different formulations of the standard that -- or a  
10 test that is applied under those circumstances, depending on the kind of  
11 invention, and we see different kinds of issues or tests that are applied for  
12 different kinds of inventions, and that's -- because of that, because it's a  
13 written description of the invention, that's necessarily a fact- based, case-by-  
14 case analysis.

15           So in our case, our invention has to do with, with re-signaling in cells  
16 through receptors, and a lot of -- I think a lot of the early work on receptors  
17 had to do with understanding that protein growth hormones inside a kind  
18 bind to their receptors and signal. And there was basic research to  
19 understand how this works, to try to understand the mechanism, and a lot of  
20 work went on to find inhibitors of this kind of signaling, inhibitors for  
21 situations like cancer or inflammation. And in fact, my company was  
22 founded to do that. Many others were. Many pharmaceutical groups  
23 worked to come up with inhibitors of signal transduction to block signaling  
24 through these receptors.

1           This invention is different. This invention has to do with providing  
2   small molecule dimerizing agents that will activate signaling, and it's, it's  
3   very different. It takes advantage of one very cool distinction. When you're  
4   trying to make an inhibitor of a receptor, it's a -- clearly, it's a -- people use  
5   actually like crystal structures, computer modeling. It's a -- it is an intensive  
6   effort of design, to design something that has the exquisite binding  
7   characteristics that will inhibit the complex structure of a given protein.

8           Our situation is different. Our situation is based on the realization that  
9   -- in part, based on the realization that a simple binder could bind. It doesn't  
10   have to bind to a specific place on a protein, on a protein receptor. It doesn't  
11   have to bind in a particular manner. The cool part is that it just has to stick.  
12   And if you have -- take an antagonist or take any molecule that sticks  
13   relatively indiscriminately, has sufficient level of affinity, just a binder, stick  
14   them together covalently and there's your dimerizing agent for a receptor.

15          And so that's, that's our invention. You've -- I know you've seen  
16   from our specification, from the background of the invention, and from the  
17   prosecution, a lot has been written about dimerization and it's mechanistic  
18   role in signaling and how you can trigger it using our -- you know, how you  
19   can come up with triggers using our, our method.

20          So to apply the written description requirement to our invention, and  
21   you have to -- to me, looking -- I think having read the cases, thinking about  
22   their inventions, then looking at our invention, I think that to apply the test  
23   you want to get into the mind of the person of ordinary skill in the art  
24   reading the document and say can this person envision this invention,  
25   examples of this invention.

1           To me, that means can this person see, envision using the different --  
2 all the different binding technologies to font, pull out a binding agent, use  
3 the description of the different receptors and different types of receptors to  
4 take molecules off the shelf that you can link together. All the different  
5 variations of carrying out the steps of our method, that is what I think is  
6 important to think about when you put yourself in the mind of the  
7 practitioner. Is that person going to think of those, those aspects of, say,  
8 Claim 8? What binding techniques do I use in my lab and whatnot?

9           And I think a lot of the cases that we read there's a lot of conjecture  
10 about what the person of ordinary skill in the art can envision when reading  
11 a given document, whether it's a DNA invention or, you know, the Cox2  
12 case. In our case we actually have, we have evidence of what the person of  
13 ordinary skill in this art does think, does imagine and does envision, and that  
14 came through in some of the papers that were cited in our prosecution. One  
15 of them is Austin, who actually says -- in talking about this dimerization  
16 approach, he actually says one can now imagine using binders to do this, and  
17 says that with the advent of modern screening technologies to find simple  
18 binders, this is now an open door, this is now something one can envision.  
19 And --

20           JUDGE MILLS: Weren't all the references that you cited in support  
21 of written description postfiling date references?

22           MR. BERSTEIN: That is Austin. I believe that's a postfiling date  
23 reference, yes.

24           MS. JARRELL: It's November '94. Austin, Qureshi, and I don't  
25 remember how to pronounce that.

1 MR. BERSTEIN: Tian. Right, Austin is November of '94. I think  
2 we have -- it's -- I think our filing date for --

3 MS. JARRELL: It's November 1st.

4 MR. BERSTEIN: We have a November 1 filing date, and Austin is a  
5 later November publication date. But the other two references are post, post  
6 that. One of them in particular is Qureshi, and in that document, that's the  
7 one where the researchers took the erythropoietin (Epo) receptor and they  
8 took one of their antagonists with competent binds to it, linked a number of  
9 those molecules together to make the dimerizing agent. It demonstrated the  
10 point of our invention with the epo receptor, and then they had a great  
11 conclusion where they actually expressed what their mental state was and  
12 what their expectations were, because they said that these data, they validate  
13 the concept both for their receptor and they also said by extension to most  
14 cited kind receptors and actually generalized it from their example.

15 And I think it's -- I think that's, that's telling because that's the actual  
16 words of somebody of skill in this art.

17 MS. JARRELL: Just to interrupt, if it's helpful, Austin was Exhibit D  
18 to the Brief.

19 JUDGE MILLS: Under what authority can we use the postfiling date  
20 references to show a written description at the time the invention was made?  
21 Didn't the Examiner discount all the exhibits that you provided because they  
22 were postfiling date references and they were not references available to one  
23 of ordinary skill in the art at the time the application was filed, so they'd be  
24 unable to support your written description argument?

1 MR. BERSTEIN: Right, but I think, I think one thing I could say  
2 about that is that the spec itself actually lays out the same point, that our  
3 spec says this. It makes the point that it's generalized, though it has the  
4 diagrams. It has diagrams that are preferably applicable to Qureshi. So  
5 these -- we have the words of our inventors who say this is the sort of  
6 structure function correlation that underlies this invention.

7 We have now a document, Austin, which is, you know, within weeks  
8 later saying much the same thing Qureshi a couple of years later -- I think  
9 Qureshi is of the late 90s. But they -- I think they're corroborating what the  
10 inventor said in their spec. It's -- it wasn't said for the first time by Qureshi  
11 and Austin and Tian. Our guys said it first. That was their -- that's their  
12 invention that they, they put this together.

13 JUDGE MILLS: Yes, you had argued in the Brief that you used  
14 competitive inhibition to link the binding domain to determine if the small  
15 dimerization molecule would competitively inhibit with ligand.

16 MR. BERSTEIN: Pardon me?

17 JUDGE MILLS: Your specification indicates that the method that  
18 you use to obtain the small dimerizing molecule is competitive inhibition  
19 with the ligand-binding domain for the receptor.

20 MR. BERSTEIN: That's one of them, yes. I mean, the specification  
21 does say you can take an antagonist and link them to -- and link two  
22 molecules together or multiple molecules together, which is what Qureshi  
23 did later. Did that answer your question?

24 JUDGE MILLS: I believe so. I was a little concerned that you had  
25 said before that your small dimerizing molecule was not really specific for



1 any location in the receptor, and then, then we have -- when you use your  
2 competitive inhibition you're actually looking for the ligand-binding  
3 domain.

4 MR. BERSTEIN: It doesn't have to. The molecule doesn't have to  
5 have the exquisite fit that an allosteric inhibitor has to have, or a ligand  
6 itself, a protein ligand. It doesn't require that, but they can be that. They  
7 can be -- you can take something that binds to any -- to many places on the  
8 protein. I think there are actually examples in some of the cited papers on  
9 using antibodies, I think with the EGFR receptor, demonstrating the point  
10 that you could have antibodies to different epitopes that caused dimerization  
11 of that receptor, and it wasn't a phenomena that required the specificity of --  
12 that's the cool part of this, that it doesn't require that kind of specificity to  
13 get your impact.

14 JUDGE MILLS: Okay.

15 MR. BERSTEIN: There are many solutions to, to that question using  
16 this approach. So -- and in this sense, I think because our method is this  
17 way, because our -- what is required to carry out this method, finding simple  
18 binders, molecules that stick, because that's -- where was I going? -- that --  
19 right. It's, it's, it's a different type of invention than a -- you know, you look  
20 at the -- I know they're not binding, but the, the training materials from the  
21 PTO have so many different examples that have been analyzed representing  
22 a lot of case law that represent a lot of different variations of different  
23 inventions that this requirement has been applied to. In our case, we're not  
24 those inventions. We're not, we're not claiming a class of compounds like  
25 Rochester. We're not claiming using a class of compounds like Rochester.

1 We're claiming a method of preparing things. And I was -- in reading  
2 Rochester, you know that the Court in Rochester said this specification, even  
3 though they didn't have one example of their selective inhibitor and they  
4 didn't show any -- they didn't try to show a structure-function relationship  
5 that the CFC said that what this specification does support are the screening  
6 methods.

7 That was clear, that screening method claims were okay, and Rochester does  
8 have their other patents. And the reason for that is the screening, that part of  
9 it was described, was adequately described that people could reading that  
10 envision ways of carrying out the screening. And I think what I'm  
11 submitting is that when the person of ordinary skill reads our document that  
12 person can envision ways of carrying out the method of preparing these,  
13 these dimerizing agents, and that should be the test. That should -- I think,  
14 that should be what we focus on: Can the person reading this actually  
15 envision ways of doing that rather than the Rochester situation? I think  
16 that's an important distinction. That's what makes it an interesting written  
17 description question, because I didn't see any other cases that were other  
18 than a substance or method of using the substance, and this is different. This  
19 is a method of preparing.

20 JUDGE GRIMES: You said that you didn't need any particular level  
21 of specificity for a site on your target proteins, but you do need to have some  
22 kind of specificity for the proteins that you're targeting, correct?

23 MR. BERSTEIN: Yeah, I think that's right. The molecule has to  
24 bind. It has to bind at some level, and the specification has some levels of  
25 affinity that --

1 JUDGE GRIMES: And, and it has to bind specifically to the two  
2 molecules that you're trying to bring together?

3 MR. BERSTEIN: Yes, it has to be able to bind to the two molecules.

4 JUDGE GRIMES: It can't be just a generic cross-linking agent  
5 because that would just cross into everything, correct?

6 MR. BERSTEIN: Right, that's right. This is not like glutaraldehyde  
7 or something, yes.

8 JUDGE MILLS: As to the binding issue that you just mentioned, I  
9 know that the record shows that there was some back and forth with the  
10 Examiner as to how the Examiner was reading the binding language and  
11 wasn't reading the binding language to encompass the affinity disclosed in  
12 the specification. Can you give us a reason why we should read the  
13 specification affinities into that binding language in the claim?

14 MR. BERSTEIN: You're referring to the art rejection?

15 JUDGE MILLS: Yes, also.

16 MS. JARRELL: It could be on versus --

17 MR. BERSTEIN: Right, I think that -- so, in reading our document,  
18 we're reading a document of cell biology, of ligands binding to receptors  
19 and molecules binding to receptors in a cell biology sense. And bind is the  
20 word that is -- is one of the words that's used in that field to describe the  
21 non-covalent bind to form a complex binding of GCSF with its receptor. I  
22 think it said GCSF binds with its receptor. Epo binds to its receptor. I think  
23 the word bind is used in this art in that sense.

24 I understand it's used -- in a bio-chemistry sense, it can be used to  
25 connote covalent detachment when that's appropriate for that context. In

1 our context, though, because we do talk about dissociation constants,  
2 because we're talking about receptor ligand interactions, I think it's very  
3 clear to the person in this art what we're talking about.

4       There, there -- certainly, there's language in the specification that we,  
5 that we would have -- we would have considered amending that language.  
6 We didn't really believe that that was necessary because of the context and  
7 the way we used the term. The specification does say "bind". You know, I  
8 think it certainly has dissociation constants which are inconsistent with  
9 covalent attachment, and it talks about binding to form complexes. And we  
10 could have amended to use other language to make that clearer if, if we  
11 thought that was important or necessary.

12       MS. JARRELL: Some of the claims actually also have the  
13 dissociation constant.

14       MR. BERSTEIN: That's right.

15       MS. JARRELL: You can't dissociate a covalent bond, so that's sort  
16 of a timative (phonetic sp.) dissonance. Not sure why the Examiner used it  
17 as a constant.

18       JUDGE MILLS: Were they -- did you argue those claims separately  
19 in the Brief?

20       MS. JARRELL: We did.

21       MR. BERSTEIN: Actually, I don't know if this qualifies for Claim  
22 differentiation, I don't know if that ever works out in a situation, but if you  
23 have a claim, a Dependent Claim that refers back to Claim 1 where in it it  
24 has a dissociation content of more than this or less than that, perhaps that  
25 does further that understanding or clarifies that that's what we're talking

1 about. We're talking about things that dissociate at some level and here in  
2 Dependent Claim whatever it's at this level.

3 I don't know if you find that satisfying an answer.

4 MS. JARRELL: It's Claim 15 that has the dissociation constant. And  
5 I'll just confirm that it is on Page -- yes, on Page 8 it indicates Claim 15  
6 stands or falls upon. In fact, actually many of the claims -- I think part of --  
7 since we are dealing with the written description and as we've said already  
8 fact-based inquiry based on what the invention is, we have many different  
9 inventions in the different claims. You have different, different scope,  
10 inventions of different scopes, so it's a different fact-based inquiry, right,  
11 some of the claims are to particular receptors, right. Claim 10, for example,  
12 calls our cited kind growth factor hormone receptors, particular sets of  
13 receptors about which there's an extensive literature binding agents that are  
14 known so on and so forth. Anyway, so, so for that reason, we had most of  
15 the claims stand and fall alone.

16 JUDGE MILLS: Okay, I believe I understand --

17 MR. BERSTEIN: Okay.

18 JUDGE MILLS: -- your position.

19 MR. BERSTEIN: Any other questions, or?

20 JUDGE MILLS: I don't think so.

21 JUDGE SCHEINER: I don't have any.

22 JUDGE MILLS: No, thank you.

23 MR. BERSTEIN: Thank you, very much.

24 JUDGE MILLS: It was very helpful.

25 MS. JARRELL: Thank you for your time.

(Whereupon, the hearing concluded at 9:20 a.m. on  
September 9, 2008.)